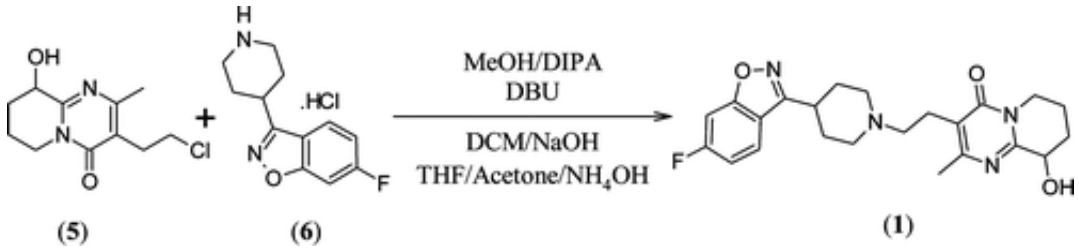
More efficient way to make popular prescription medication

January 23 2013



In a demonstration of the power of green chemistry, scientists are reporting development of a new and more efficient process for making one of the most costly and widely used medications for severe mental illness. Described in a report in the journal *ACS Sustainable Chemistry & Engineering*, it produces larger amounts of the medication than the existing commercial process while reducing the use of solvents and other potentially toxic substances.

Vijayavitthal T. Mathad and colleagues point out that paliperidone, marketed under the brand name Invega, is one of a new generation of medicines for schizophrenia, a severe form of mental illness. Paliperidone has advantages over other medicines, but the current process for making it is expensive and inefficient, contributing to the drug's cost—about $18 per tablet in the United States. The process also requires use and disposal of large amounts of solvents that require

special handling.

They describe development of a new recipe for making paliperidone. It not only yields larger amounts of the medicine, but uses less solvent and involves an innovative and environmentally friendly method for purifying the medication and for the control and removal of critical impurities that result from the process and carryover from raw materials. The sustainability of the process lies in its capability to withstand the cost pressure when the drug becomes completely generic, the authors said. Reducing the raw material cost not only makes it sustainable but it should be environmentally and production-friendly.

More information: "An Improved and Efficient Process for the Production of Highly Pure Paliperidone, a Psychotropic Agent, via DBU Catalyzed N-alkylation", *ACS Sustainable Chem. Eng.*, DOI: 10.1021/sc3000916

Abstract
The present work describes an improved and efficient process for the synthesis of paliperidone (1), an antipsychotropic agent. The synthesis comprises the DBU (1,8-diazabicycloundec-7-ene) catalyzed N-alkylation of 3-(2-chloroethyl)-9-hydroxy-2-methyl-6,7,8,9-tetrahydro-4 H-pyrido[1,2-a]-pyrimidin-4-one (5) with 6-fluoro-3-piperidin-4-yl-1,2 benzisoxazole hydrochloride (6) in methanol as the solvent and diisopropylamine as a base to yield paliperidone (1) with 85% yield and over 97% purity by HPLC. The present work also describes an industrially efficient purification process for the removal of critical process related impurities (8 and 9) in paliperidone (1). The process furnished 1 with an overall yield of about 60% and 99.85% purity.

Provided by American Chemical Society